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Megaloblastic Anaemia – Clinical Spectrum and Haematological Profile in a Tertiary Care Center of North India

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ABSTRACT

Background - Anaemia is the most common nutritional deficiency disorder in the world. It affects all age groups but the most vulnerable are preschool-age children, pregnant women, and non-pregnant women of childbearing age. In India, anaemia affects an estimated 50% of the population. The megaloblastic anemia is a common disease with varied presentation. Megaloblastic anaemia is caused by vitamin B12 and/or folic acid deficiency.

Aims and Objectives - The aim of the present study is to evaluate the clinical and haematological parameters of patients with megaloblastic anaemia.

Material and methods - A 1 year retrospective study was conducted in the Department of Pathology, PGIMS, Rohtak to correlate the clinical and haematological findings of megaloblastic anaemia.

Results - A retrospective study was conducted from October 2017 to September 2018. A total of 641 cases of bone marrow aspirations were studied. Among them, 202 cases were of anemia and 86 confirmed cases were of megaloblastic anaemia. The highest incidence was seen in the age group of 10-15 years with male : female ratio of 1:2. Most common presenting symptoms were weakness, fatigue, dyspnoea followed by jaundice with signs of pallor and hepatosplenomegaly. 56.9% of cases have less than 7g/dl haemoglobin and 47.6% have MCV of 100-120fl. On bone marrow aspiration, erythroid hyperplasia was seen in 81.4% cases, dysmyelopoiesis in 25.5% cases and increase iron grade in 24% cases.

Conclusion - Megaloblastic anemia is one of the common causes of undiagnosed anemia. Prompt diagnosis is important as it is a completely curable condition and also to prevent the complications associated with the disease.

Keywords: Megaloblastic anemia, Vitamin B12, Folic acid, Haematological parameters, Bone marrow aspiration.

INTRODUCTION

Megaloblastic anemia is defined as macrocytic anemia that is usually caused by deficiency of vitamin B12 and/or folic acid.[1] But it may arise because of inherited or acquired abnormalities affecting the metabolism of these vitamins resulting in abnormal nuclear maturation with normal cytoplasmic maturation, apoptosis, ineffective erythropoesis, intramedullary hemolysis, pancytopenia and typical morphological abnormalities in blood and marrow cells.[2] It is an important reversible cause of neurodevelopmental deterioration.[1] Macrocytosis is observed in 1.7-3.6% of patient underlying routine haematological investigations.[3] Macrocytosis is not accompanied by anemia in about > 50% of cases. Macrocytosis usually precedes anemia, and may be an indicator of early vitamin B12 or folic acid deficiency.[4] Hence, isolated macrocytosis should always be investigated.

The present study was carried out to evaluate the varied clinico-hematological parameters along with bone marrow aspiration findings of Megaloblastic anemia.

MATERIAL AND METHOD

This retrospective observational study was conducted in the Department of Pathology, Pt. BDS PGIMS, Rohtak from October 2017 to September 2018. A

total of 641 cases of bone marrow aspirations received in that year were screened. Out of which 202 cases diagnosed with anemia were selected. Those diagnosed with Aplastic anaemia and Iron deficiency anaemia were excluded from the study and a total of 86 bone marrow aspiration confirmed cases of megaloblastic anaemia were selected for study group. Detailed clinical history, complete blood count, peripheral blood smear findings and bone marrow findings were noted. The data were collected, and multivariate analysis was done to determine the correlation between symptoms, signs, and hematological investigations.

2ml of EDTA blood was collected for complete blood counts using BC-6800 MINDRAY. Bone marrow aspirations were performed using Salah's needle from iliac crest region. Peripheral blood film and Bone marrow aspiration smears were stained with Leishman's stain. Perl's stain for Iron grade was done on the bone marrow smears. Descriptive statistics was analyzed with SPSS version 17.0 software.

RESULT

A retrospective study was conducted from October 2017 to September 2018. A total of 641 cases of bone marrow aspirations were received during the year. Out of which 202 cases were of anaemia, 86 cases of megaloblastic anemia (42.57%) proven on bone marrow aspiration over the one year period. Out of 86 cases of megaloblastic anemia, 29 were males and 57 were females with a Male to Female ratio of 1:2. The age of the patients ranged from 4 months to 79 years with maximum number of patients were in the age group of 10-15 years. Age distribution is shown in figure 1.

The most common symptom at presentation were related to anaemia (weakness, fatique, dyspnoea) constituting 72 out of 86 cases (83.7%) followed by jaundice (25.6%) and bleeding manifestation (17.4%). The frequency of symptoms are listed in table 1. On clinical examination, pallor was present in 60 cases (69.8%) ranging from mild to severe. Hepatomegaly was observed in 25 cases (29%) followed by 21 cases (24.4%) of spleenomegaly. Other signs are discussed in table 2.

Complete haemogram was done on 5 part automated hematology analyzer (MINDRAY). Mean Hemoglobin was 6.45gm/dl. 49 patients (56.9%) had severe anemia (Hb < 7g/dl). Out of them blood transfusion was required in 20 patients (23.2%). Mean MCV was 104.5fl. Maximum number of patients had MCV in 100-120 fl range. Average MCH was and MCHC was 31.84 pg and 32.52 g/dl.

In peripheral blood film examination, 84% of cases showed predominantly macrocytosis, hypersegmented neutrophils with macro-ovalocytes and mild to moderate anisopoikilocytosis. Other abnormalities were tear drop cells, basophilic stippling, polychromasia and cabot's rings.

Bone marrow aspiration were predominantly hypercellular with erythroid hyperplasia. Myeloid erythroid ratio (M:E) was reversed, varied from 1:1 to 1:6. Dysmyelopoiesis was observed in 30 cases with giant metamyelocytes and increase in size of myelocytes and promyelocytes. 14 cases with dyserythropiesis showed features of nuclear budding, multinuclearity and megaloblastoid change.

Iron grades were reduced (grade 0- 1+) in 31 cases (36%) and were normal to increased (grade 2+ to 6+) in 26 cases (30.2%).

DISCUSSION

Megaloblastic anemia is a distinct type of anemia characterized by macrocytic RBCs and typical morphological changes in RBC precursors. The RBC precursors are larger than the cells of same stage and exhibit disparity in nuclear-cytoplasmic maturation.[5]

Megaloblastic anemia is a panmyelosis, where erythroid hyperplasia is a prominent feature. The morphologic hallmark is nuclear-cytoplasmic dissociation, which is the best appreciated in precursor cells in the bone marrow aspirate. Neutrophils with characteristic hypersegmented nuclei appear in the blood early in the course. As megaloblastic anemia progresses, neutropenia and thrmocytopenia develop. [4]

In the present study, highest incidence was seen in the age group of 10-15 years with M: F ratio of 1:2 which is in concordance with studies done by Kaur et al [2] and Yellinedi et al [6]. Other studies done by Chan et al [7], Baik et al [8] and Charke et al [9] had reported highest incidence in older age groups with an equal sex ratio or male preponderance.

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In our study, mean Hemoglobin was 6.45gm% which is smiliar to the Hb reported by Zengin et al who also reported the mean hemoglobin as 6.4 g/dL.[10] Mean MCV in our study is 104fl. Other studies done by Williams et al and Mandloi et al also reported mean MCV of 102fl and 105fl, respectively which is similar our study. [11]

The present study revealed the most common presenting symptom to be Weakness, fatigue, dyspnoea (83.7%) and Jaundice (25.6%) which is comparable with the study done by Unnikrishnan et al[3]. Bleeding manifestation was noted in 17.4% of cases in our study which could be most likely due to thrombocytopenia. Previous studies had documented bleeding in 17% to 20% of patients in megaloblastic anaemia. Fever was seen in 15.1% of patients in our study, the commonest cause being infection to which the individual is much more susceptible in this disease due to impaired intracellular killing of ingested bacteria by neutrophils and macrophages.[12] Symptoms are related to the pancytopenia which is due to impaired DNA synthesis resulting in ineffective erythropoiesis.

In our study, Pallor was seen in 68.8% which is much lower than reported by other studies. Studies have reported 98.8% - 100% of patients presenting with pallor.[2] Spleenomegaly and hepatomegaly were present in 24.4% and 29% cases of cases in the present study which is comparable to the study done by Mandloi et al[11]. Gomber et al [13] reported hepatomegaly in 66 % of cases which is much higher than the present study. Splenomegaly was present in most of the moderate to severe anemic and thrombocytopenic patients. It is generally believed that as severity of anemia increases, thrombocytopenia develops followed by neutropenia.[11]

30.2% of the cases needed blood transfusion secondary to severe anemia in a study conducted by Yellinedi et al[6] and Gomber et al[13], whose percentage is higher in the present study as Vitamin B12 is necessary for red cell maturation.

In the Indian scenario, where assays for methyl malonic acid and homocysteine are expensive and not readily available, we feel that screening blood films for hypersegmented neutrophils is useful for detecting early megaloblastosis.[14] Due to limited resources and financial constrain, Serum Vitamin B12 and Folic acid levels assay could not be done.

CONCLUSION

Megaloblastic anemia is one of the common causes of undiagnosed anemia. Due to poor nutrition and strict vegetarian diet, Vitamin B12 deficiency was the most common cause of megaloblastic anaemia. Not only raised MCV, but normal MCV and macrocytosis on peripheral smear should also be considered to evaluate magaloblastic anaemia. Neutropenia is a common concomitant finding in megaloblastic anemia and can be associated with leucopenia. A correct diagnosis and prompt therapy lead to a complete and an eventful recovery.

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Figure 1: Age Distribution of patients

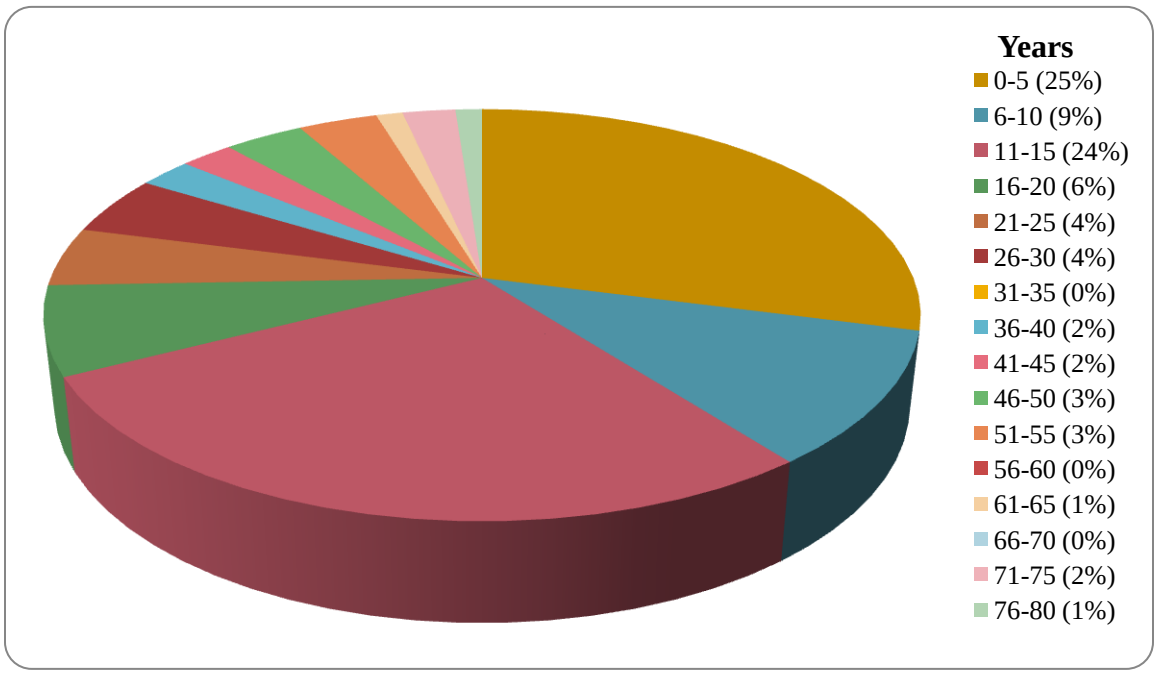

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Table 1: Symptoms at presentation

	No. of cases (N=86)	%
Related to anaemia (Weakness, Fatigue, Dyspnea)	72	83.7
Yellowish discoloration/ Jaundice	22	25.6
Bleeding manifestation	15	17.4
Fever	13	15.1
Abdomen Pain	12	13.9
Neurologic manifestation	7	8.1
Decreased appetite	5	5.8
Swelling of feet	4	4.6
Weight Loss	2	2.3
Pruritis	1	1.2
Diarrhea	1	1.2

Table 2 – Signs at presentation

	No. of cases (N=86)	%
Pallor	60	68.8
Hepatomegaly	25	29
Spleenomegaly	21	24.4
Icterus	14	16.3
Bony tenderness	08	9.3
Neurologic Manifestation	06	7
Lymphadenopathy	05	5.8
Failure to thrive	04	4.6
Edema	02	2.3
Skin changes	02	2.3
Glossitis	01	1.2
Clubbing	01	1.2

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Table 3 – Hematological parameters

	Range	Mean ± SD
Hb (g/dl)	2.5-14.3	6.45 ± 2.43
Hct (%)	8.3-36.5	20.89 ± 7.21
RBC ($\times 10^{12}$ cells/L)	0.98-4.14	2.03 ± 0.75
MCV (fl)	76.1-153.4	104.50 ±14.38
MCH (pg)	22.1-41.5	31.84±3.91
MCHC (g/dl)	24.2-36.4	32.52±2.43
RDW-CV (%)	12.5-45.4	23.40 ± 6.53
TLC ($\times 10^3$ /µl)	1,300-40,000	7,214.53±7,845.96
APC ($\times 10^5$ /µl)	12,000-4,45,000	35,012.17± 31,452.23
Reticulocyte count (%)	0.1-13.6	4.08±3.50

Table 4 – Bone marrow aspiration findings

	No. of cases	%
Erythroid hyperplasia	70	81.4
Megaloblastic erythropoiesis	66	76.7
Dysmyelopoiesis	30	25.5
Dimorphic erythropoiesis with megaloblastoid change	20	23.3
Dyserythropoiesis	14	16.3
Increased eosinophilic precursors	12	18.6
Pancytopenia	12	23.2
Dysmegakaryopoiesis	6	6.9
Bicytopenia	4	4.7

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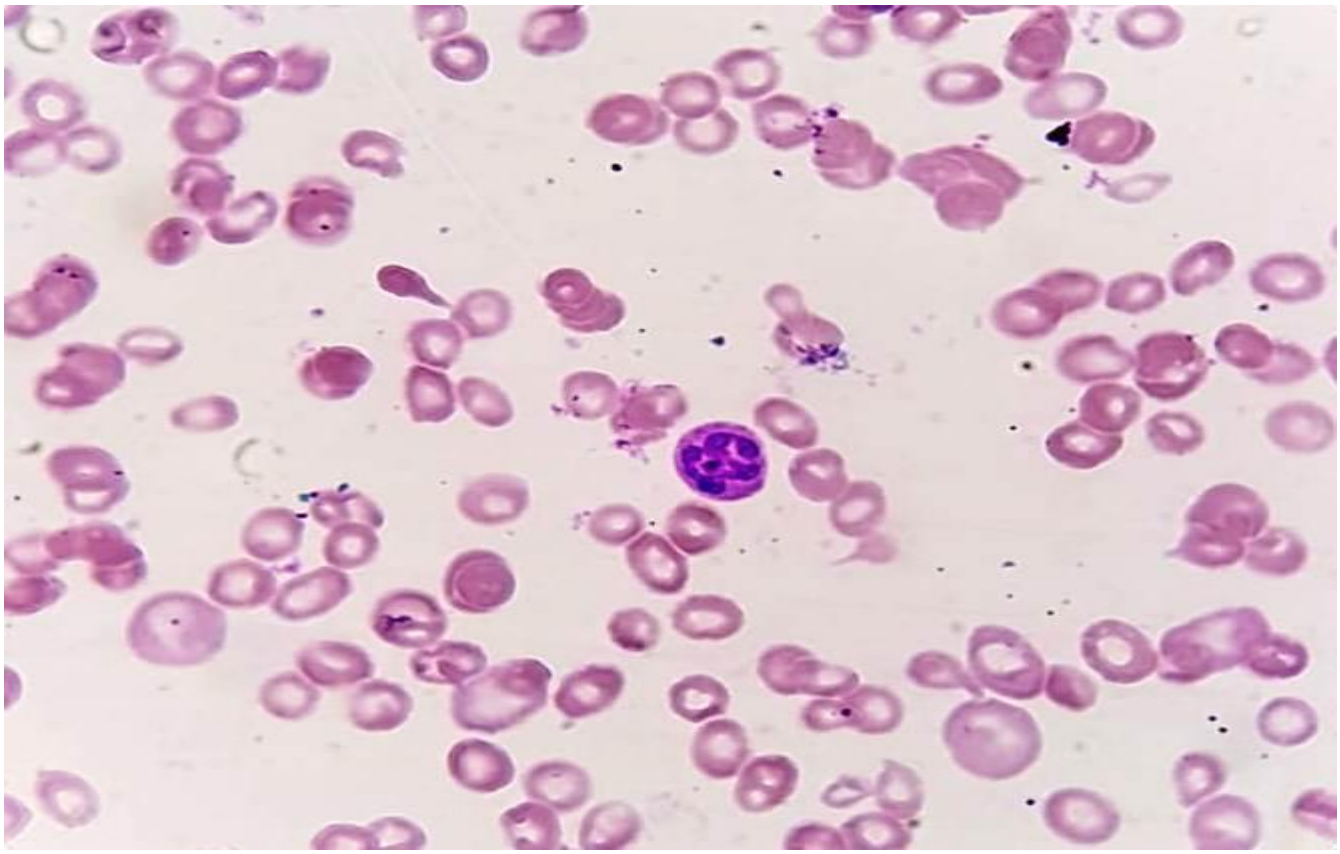

Figure 2: Peripheral blood film showing macrocytic picture with macro-ovalocytes and hypersegmented neutrophil

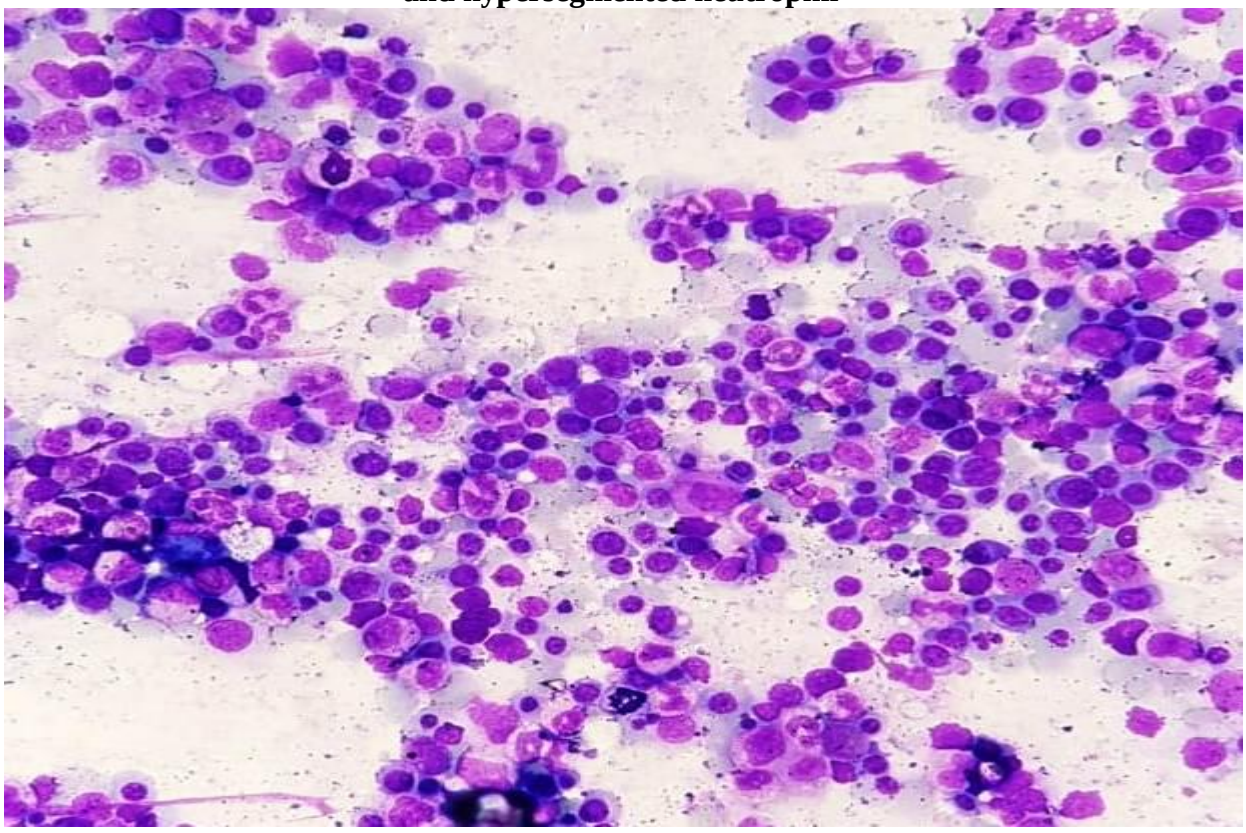

Figure 3: Bone marrow aspiration smear showing erythroid hyperplasia with megaloblastoid change

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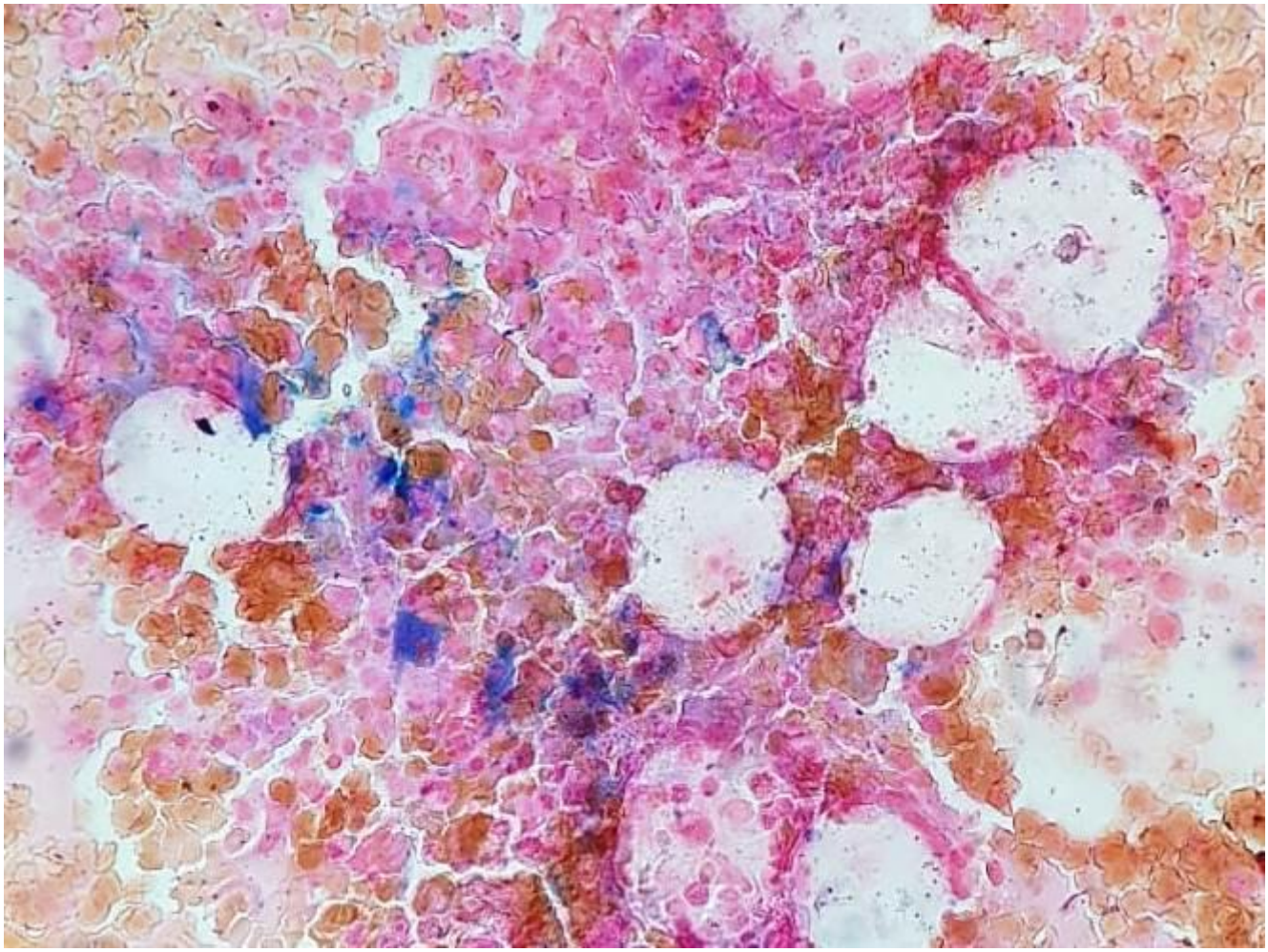

Figure 4: Perl's stain on bone marrow aspirate demonstrates increased iron stores

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